CLEAN-IN-PLACE

AUTOMATION -

GLATT COATING PAN APPLICATION
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1. **Summary**

The primary objectives of this cleaning study was to ascertain the feasibility of conducting automated Cleaning-In-Place (CIP) of a Glatt coating pan and to prove that the CIP cleaning concept was truly an automated, repeatable process.

The cleaning study was performed on a Glatt GCX 1500 with a setup consisting of a MORK Mobile CIP Unit, and one (1) 360° spray device.

The cleaning study included preliminary cleaning trials that clearly showed that it is feasible to automatically clean the coating pan and the associated transfer lines with a MORK CIP system and a spray device setup.

Based upon the results of the cleaning study, it can be concluded that it is feasible to achieve the following goals:

- Improved cleaning of the coating pan.
- Automatic cleaning of the transfer piping.
- Confirmation of cleanliness of the CIP skid without manual intervention.
- Improved GMP compliance by means of automated cleaning.
- Highly improved & safer working environment for personnel.
- Reduced labor hours for cleaning.
- Introduction of a repeatable and validateable CIP system.
2. **INTRODUCTION**

2.1 **Background**

As requested by the Customer - **MORK Process** initiated a cleaning study in order to test and demonstrate the use of a **MORK** Mobile S Series CIP Unit for the cleaning a deposit of Eudragit NE30D and TiO₂ from a Glatt coating pan. (NE30D was sprayed at first, followed by the TiO₂). This coating pan was processing an under-filled batch of tablets, so there was a considerable amount of over-spray on the sides of the pan. The Eudragit polymer was allowed to harden and cure prior to testing. Prior to cleaning, the material resembles a hard, uniform deposit, resembling a white hazy buildup on vessel surfaces. Near the nozzle ports, the material tends to clump together. The Customer had requested that the coating pan as well as the transfer lines be successful cleaned in place. These transfer lines processed NE30D for approximately one day, followed by a batch of TiO₂. The Customer’s objective for a CIP system is remove this deposit since manual cleaning takes an excessive amount of time, is hazardous to the operators, and very difficult to accomplish with any type of repeatability or reproducibility.

2.2 **Scope**

The scope of the cleaning study included:

- On-site engineering study on the coating pan with product for an extended period of time. This included a systematic evaluation of the internal coating pan & gun components, such as critical areas and hot spots.
- Preparation of the on-site cleaning trials, which included supply of necessary fittings, tools, identification, and supply of spraying devices, etc.
- Series of cleaning trials utilizing actual material residue in order to optimize system set up. This included installation and adjustment of a custom spray device in order to achieve:
  - Highest level of physical impact on all surfaces
  - Wetting intensity and coverage
- Preparation for “worst case” cleaning scenario.
- Preparation of the Cleaning Study Report.
2.3 Objectives

The primary objective of this cleaning study was to ascertain the feasibility of conducting automated Cleaning-In-Place (CIP) of the Glatt GCX 1500 coating pan and associated transfer piping utilizing a MORK S Series Mobile CIP Unit and associated spraying devices. In addition, the automatic cleaning of the Mobile CIP skid was also to be demonstrated.

2.4 Success Criteria

The success criterion for the cleaning study is to demonstrate that it is feasible to automatically clean the Glatt coating pan. Results were based purely on visual inspection of all internal components. This was feasible since the coating pan could be fully viewed between cleaning runs for close inspection.

Ultimately, however, the success criteria of implementing an automated CIP system are the achievement of the following goals:

- Improved GMP compliance by means of automated cleaning
- Highly improved, and safer, working environment for personnel
- Reduced labor hours for cleaning
- Introduction of a repeatable and validateable CIP system
- Cleaning of the coating pan.
- Automatic cleaning of the transfer piping
- Cleanliness of the CIP skid without manual intervention.
3. TESTING ANALYSIS

3.1 Cleaning Procedure

The **MORK** Mobile S Series CIP Unit was connected to the utilities available at the Customers’ North American facility. These utilities included 480 volt power, compressed air supply (+90 psi), city water, drain connection for waste water, and coating pan supply and return lines. The connections to the vessel and gun assembly were 1” flexible hoses, including the typical transfer piping which included both 5/8” SS lines and flexible nylon 5/8” hoses.

An application specific rotating cleaning nozzle was installed using the available CIP port in the center of the coating pan. Although one nozzle may have been sufficient, the addition of a second nozzle may help to decrease the overall cleaning time. This CIP jet-head nozzle was located relatively high up in the vessel, to ensure the backsides of the baffles had sufficient impingement. Rotation of the coating pan enhanced the cleaning action and ensured that all surfaces had access to the impingement effects of the CIP nozzle.

Two different trials were tested for CIP cleaning using the same vessel. The first coating pan trials were performed on what the Customer deemed the worst case. This included multiple layers of NE30D and TiO₂ dried on to the coating pan.
3.2 Layout of test vessel

- Front door of vessel.
- 6 nozzles from gun being cleaned.
- Zone #2 – Jet head nozzle for pan cleaning.
- Front of Coating Pan
- Stainless piping
- Zone #1 Supply – transfer pipes
- Jet head nozzle
3.3 Pictorial set-up of test area.

MORK Mobile CIP skid set up in test room. Yellow line is air supply, blue hoses supply zones #1 and #2. The white hose is the return from the coating pan / drain. The black cord is 480 volt power and the red line was fresh water inlet.

Transfer piping loop for stainless steel lines and flexible hoses. All connected to the gun manifold.
Rotary Impingement nozzle in upper right corner for cleaning coating pan. Pan was rotated at 2 rpm during cleaning for optimal surface coverage.
3.4 Summary of Low-Pressure Tests – Day #1

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rinse #1</td>
<td>80 liters, elevated temperatures and pressures. Each zone was operated for approximately 5 minutes with water exiting straight to drain.</td>
</tr>
<tr>
<td>Rinse #2</td>
<td>120 liters water at elevated temperatures and pressures through Zones #1 and #2. All water once-through.</td>
</tr>
<tr>
<td>Rinse #3</td>
<td>100 liters of water were run through Zone #1 for 5 min and Zone #2 for 22 minutes. Recirculation.</td>
</tr>
<tr>
<td>Wash #1</td>
<td>100 liters water mixed with CIP 100. Zone #1 run for 5 min, Zone #2 for 30 min.</td>
</tr>
<tr>
<td>Wash #1A</td>
<td>100 liters fresh water mixed with CIP 100. Zone #1 run for 65 min and Zone #2 for 70 min (temp increased for Zone #2 run).</td>
</tr>
<tr>
<td>Rinse #4</td>
<td>150 liters water. – Recirculation for 5 min within each zone.</td>
</tr>
<tr>
<td>Wash #2</td>
<td>100 liters water mixed with CIP 200. 30 min run in Zone #1 and 20 min within Zone #2</td>
</tr>
<tr>
<td>Rinse #5</td>
<td>200 liters city water – once through each zone.</td>
</tr>
</tbody>
</table>

Zone #1 – Defined as transfer piping and gun manifold
Zone #2 – Defined as internal impingement nozzle for interior cleaning of coating pan.
3.4.1 Observations

Prior to CIP rinse
Initially, the material in the Glatt coating pan represented a very hard white layer, most prominently around the conical section of the vessel. The whitish NE30D was not removable by gently scraping with a fingernail. A considerable amount of the holes in the Glatt coating pan were clogged with material. The material did exhibit a melting or softening tendency when heated and hydrated.

Internal to the piping, a hazy buildup was visible. This haze was removable when wiping with the finger.
Prior to starting the cleaning trials.

Note the many occluded holes in pan.
3.4.2 Results for Day #1

**Rinse #1 Result**
The use of cold water did not have any effect on the dilution of the material (as expected). When the rinse water was observed, there were minimal traces of dissolved material present.

**Rinse #2 Result**
A fresh 200 liter batch of hot water was prepared. This water was run through the system as a once-through operation. Both Zone #1 (transfer piping) and Zone #2 (the vessel cleaning portion) were flushed. The duration of this rinse was not sufficient to dislodge the material, and it was determined that additional cleaning time would be necessary. The transfer piping (including the stainless steel lines, Teflon tubing and silicon rubber hose) was cleaned at a lower pressure, due to the temperature and pressure limitation of the flexible hose.

**Rinse #3 Result**
A fresh 100 liter batch of water was prepared. This hot water recycle Rinse was run for 5 minutes through Zone #1 and 22 minutes through Zone #2. After this Rinse was completed, the CIP water in the buffer tank appeared dirty – some clumping also started to occur, mostly in the outer sections of the Glatt vessel and in the CIP buffer tank. After this Rinse, the water was drained.

**Wash #1**
A fresh 100 liter batch of CIP water was heated and CIP 100 was added to the batch. The wash water was run through Zone #1 at for 5 minutes and Zone #2 for 30 minutes.

After this initial wash, the product appeared to start becoming dis-lodged by showing signs of streaking. The CIP buffer tank was once again dirty and cloudy. Streaks occurred when the buffer tank was allowed to dry. Chunks of material were more prevalent in the Glatt screen area. The piping also appeared to still have residue which was easily visible and could be wiped off by finger-touch.

Although NE30D can not be dissolved directly in any alkaline or acidic solution, it can be softened and caused to swell by means of an alkaline wash. The combined effect of the swelling and the direct water impingement affects the cleaning of the Eudgrait as was observed during this run and all other successive wash runs (wash being defined by use of a cleaning agent).
Wash #1A
The wash function with CIP 100 was continued. A fresh 100 liter batch of water was heated and CIP 100 was added. Zone #1 was washed for 65 minutes and Zone #2 was washed for 70 minutes.

After washing – the water in the CIP buffer tank again appeared dirty and cloudy. The material also coagulated inside the Glatt pan and lightly adhered to the screen area of the outer vessel. These chunks were gummy-like in nature and could be easily removed by hand or spatula.

Rinse #4 Result
150 liters of fresh water was introduced to the buffer tank and heated. This liquid was sprayed for 5 minutes in Zone #1 and 5 minutes in Zone #2. All water was then sent to drain.

The observation after this rinse showed that considerable cleaning took place. Most of the pan areas were visually clean.
Wash #2 Result
A fresh 100 liter batch of water was prepared with Steris CIP 200 added to this batch. The cycle was run for 30 minutes through Zone #1 and 20 minutes through Zone #2 with a higher temperature used on Zone #2.

Inspection of the vessel walls revealed that all traces of the NE30D material were removed from the tank. After the cycle was complete, some minor clumps of the whitish material (most likely NE30D) were observed in the CIP buffer tank.

Rinse #5 Result
200 liters of water was introduced to the buffer tank and heated.. This liquid was sprayed into the coating pan as a once through pass, simply to rinse the remaining CIP 200 liquid out for safer inspection.

This fresh water rinse revealed a clean surface, no residuals visible inside the coating pan surfaces. Only some of the chunks of the material caught by the Glatt coating pan screen were visible, but still easily removed by hand while hot.

All flexible hoses from the transfer piping appeared clean of NE30D and TiO₂.
All surfaces clean of Eudgrit NE30D polymer. 

*Note the clump of material* – this could be easily removed by hand while still warm. Occluded holes in this photo are only water. After drying, ALL coating pan holes were open.
Loop set-up of the 5/8” SS piping for cleaning trial. Elevated temperatures and higher pressures were used.
3.4.3 Observations

Prior to CIP rinse
The piping on day #2 had a visible trace of the Ti02 and NE30D mixture present. This was confirmed by a boroscopes inspection and visual confirmation. The three pipes were assembled in series, but this time without any pressure and temperature limiting flexible lines.

3.4.4 Results for Day #2

Rinse #1 Result
The use of a once-through hot water rinse simply was used to heat up the transfer piping for proper CIP cleaning.

Wash #1 Result
A fresh 80 liter batch of water was heated and CIP 100 was added. The CIP water was re-circulated in the loop for 60 minutes.

After washing – the buffer tank appeared to be somewhat dirty and cloudy. This clearly indicated that cleaning was occurring.

Rinse #2 Result
A flush with fresh water was to make inspection of the piping possible without the presence of CIP 100.

Inspection at this point revealed that the elevated temperature and pressure was successful in cleaning the stainless piping. The visible residue was gone from the surface when inspected using a light.

Wash #2 Result
A fresh batch of 80 liters of water was heated and CIP 200 was added and circulated through the transfer piping for 30 minutes.

Rinse #3 Result
200 liters of water was flushed through the transfer piping to flush out the remaining CIP 200. Upon inspection using the boroscope, the pipe walls were free of coating material.
Stainless steel pipe – prior to cleaning.

Stainless steel pipe – after cleaning.
### 3.5 Additional observations of cleaning the Glatt R&D Coating pan

<table>
<thead>
<tr>
<th>Hot Spot / Critical Area</th>
<th>Observations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coating pan baffles</td>
<td>This area is difficult to reach for the CIP nozzle if located in the center of the tank. For this reason, the impingement nozzle was offset to the top and the pan was rotated.</td>
</tr>
<tr>
<td>Exterior areas of the coating pan</td>
<td>All parts exterior to the pan were not focused on for cleaning. These also could be easily cleaned, but the addition of several spray nozzles behind the side access panels would be required. Since this is not product contact, cleaning of this area was not focused on.</td>
</tr>
<tr>
<td>CIP Unit</td>
<td>It is critical that the CIP unit does not become a cleaning issue. After the cleaning runs, several internal rinse cycles were conducted. Inspection showed that the unit was then free of residue.</td>
</tr>
<tr>
<td>Transfer piping</td>
<td>As with the coating pan, the transfer piping must be equally clean. It is essential that the flowrate and turbulence be maintained. In addition, the temperature must be elevated for sufficient removal of the NE30D powder and the TiO₂.</td>
</tr>
</tbody>
</table>
4. CONCLUSION

The cleaning study clearly showed that it is feasible to automatically clean the Glatt XC 1500 coating pan with a MORK S Series CIP system. The trial was performed after an under filled / overspray condition was processed – utilizing a setup consisting of the following:

✓ One MORK Mobile CIP Unit
✓ Flexible hoses
✓ One CIP nozzle
✓ Transfer piping loop

Based upon the results of the cleaning study, the following CIP concepts are feasible and will obtain the expected cleaning result. Details shall be evaluated during a Basic Design of a system:

<table>
<thead>
<tr>
<th>CIP CONCEPT</th>
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<tbody>
<tr>
<td><strong>System Description</strong></td>
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<td></td>
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<tr>
<td><strong>Expected CIP cycle</strong></td>
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<tr>
<td><strong>Total expected max cleaning time</strong></td>
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</tbody>
</table>
The table below gives an overview of the water consumption and the elapsed cleaning time for the product cleaning trial.

<table>
<thead>
<tr>
<th></th>
<th>Summary of Cleaning Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water Consumption</td>
<td>~ 950 liters (250 gallons)</td>
</tr>
<tr>
<td>CIP Rinse flow</td>
<td>Approximately 15 gpm</td>
</tr>
<tr>
<td>Temperature</td>
<td>Elevated CIP fluid</td>
</tr>
<tr>
<td>Actual CIP cleaning time</td>
<td>~ 100 min - not including heating time or visual inspections.</td>
</tr>
</tbody>
</table>